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PATENT COOPERATION TREATY

PCT

Rec'd PCT/PTO 18 MAR 2005

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Artcle 36 and Rule 70)

Applicant's or agent's file reference PC03009-LG	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. **PCT/KR2003/001932**	International filing date *(day/month/year)* **22 SEPTEMBER 2003 (22.09.2003)**	Priority date *(day/month/year)* 26 SEPTEMBER 2002 (26.09.2002)

International Patent Classification (IPC) or national classification and IPC

IPC7 C07F 9/6561, C07F 9/6509, A61K 31/675

Applicant

LG LIFE SCIENCES LTD. et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demamd	Date of completion of this report
22 MARCH 2004 (22.03.2004)	15 FEBRUARY 2005 (15.02.2005)
Name and mailing address of the IPEA/KR Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer KIM, YONG Telephone No. 82-42-481-8148

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

ational aplication No.
PCT/KR2003/001932

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed

☐ the description:
pages _____ , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☐ the claims:
pages _____ , as originally filed
pages _____ , as amended (together with any statment) under Article 19
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☐ the drawings:
pages _____ , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☐ the sequence listing part of the description:
pages _____ , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application(under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide** and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained inthe international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disc losure in the international applicationas as filed has been furinshed.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box(Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed." and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.*

INTERNATIONAL [redacted] LIMINARY EXAMINATION

[redacted]national aplication No.
PCT/KR2003/001932

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-11	YES
	Claims	None	NO
Inventive step (IS)	Claims	5, 7-9	YES
	Claims	1-4, 6, 10, 11	NO
Industrial applicability (IA)	Claims	1-11	YES
	Claims	None	NO

2. Citations and explanations (Rule 70.7)

Reference is made to the following document:

D1: WO 02/57288 A1 (25 Jul. 2002)

The present invention relates to (+)-trans isomers of 1-(phosphonomethoxy-2-alkylcyclopropyl)methyl nucleoside derivatives, a process for the preparation of stereoisomers thereof, and the use of antiviral agents thereof.

D1 which is considered to represent the most relevant state of the art, disclose acyclic nucleoside phosphonate derivatives, and a process for the preparation of the same.

1. Novelty

Although both the compounds of the present invention and D1 have the same structure, the compounds of claims 1 to 4, 6, 10 and 11 are novel in that they are (+)-trans isomers(enatiomer), whereas the compounds of D1 are racemates which contain all possible stereoisomers((+) or (-)-trans enatiomer, diastereomer).
Since the compositions of claims 10 and 11 are characterized by the novel compounds of claims 1 to 4, they are also novel. Moreover, a process for preparing the claimed compounds of claims 5 and 7 to 9 is also novel.
Consequently, the subject matter of the present claims 1 to 11 is considered to be novel under PCT Article 33(2).

2. Inventive Step

(+)-Trans isomers of 1-(phosphonomethoxy-2-alkylcyclopropyl)methyl nucleoside derivatives of claims 1 to 4 and the intermediates of claim 6 are structurally very close to the compounds of D1 in that they are just (+)-trans isomers(enatiomer) of the compounds of D1 which are racemates which contain all possible srereoisomers.
Furthermore, it is not considered that the compounds of claims 1 to 4 show more potent antiviral activity than the compounds of D1(see the Table below).

(Continued on supplemental box)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of:

Box V

[Table]

	Compd. No.	Substituents					EC_{50}(μM) in HBV	CC_{50}(μM) in HepG2.2.25
		X^1	X^2	R^1	R^2	R^3		
Present invention	1	OH	NH_2	CH_3	H	H	0.03	>1000
	2	H	NH_2	CH_3	H	H	1.0	>1000
D1	97	OH	NH_2	CH_3	H	H	>0.05	>1000
	98	H	NH_2	CH_3	H	H	>1.0	>1000

Since the compositions of claims 10 to 11 are characterized by the non-inventive compounds of claims 1 to 4, the compositions of these claims also lack inventive step.

Consequently, the subject matter of the present claims 1 to 4, 6, 10 and 11 lacks an inventive step under PCT Article 33(3).

3. Industrial Applicability
There is no reason for denying industrial applicability of this invention. Consequently, claims 1 to 11 appear to meet the requirement of PCT Article 33(4).